MODELING OF A COMPLEX OF SYSTEMS OF THE ORGANISM WHICH ARE ASSOCIATED WITH BLOOD CIRCULATION AND CARRYING OUT OF PHYSIOLOGICAL EXPERIMENTS WITH THIS COMPLEX

L. A. Dartau

Translation of "Modelirovaniye kompleksa sistem organizma, svyazannykh s krovoobrashcheniyem, i vosproizvedeniye na nem fiziologicheskikh eksperimentov," in: Optimization Study of Operations. Bionics (Optimizatsiya. Issledovaniye operatsii. Bionika), edited by Ya.Z. Tsypkin, Moscow, "Nauka" Press, 1973, pp. 229-235

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16. Abstract A computer model of a complex of systems associated with blood circulation is discussed and illustrated with a diagram. Modeling and physiological tests are discussed, data are presented and comparisons of modeling and physiological tests are presented, for forced hypo- and hyperventilation, administration of arfonad and isolated perfusion of the carotid sinus. A model experiment in regulation of an artificial heart is described and discussed, with a comparison of four control algorithms.

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MODELING OF A COMPLEX OF SYSTEMS OF THE ORGANISM WHICH ARE ASSOCIATED WITH BLOOD CIRCULATION AND CARRYING OUT OF PHYSIOLOGICAL EXPERIMENTS WITH THIS COMPLEX

L. A. Dartau

Modeling of various physiological systems is extensively used at the present time, for study of the operation of these systems, both statically and dynamically. The majority of models describe the activity of individual, isolated systems and study their behavior, under one set of values of input quantities and independent variables or another affecting the nature of operation of the system. Such models hardly include all the models described in works [1-3]. As a rule, in creating similar models, they are based on the fact that a given system is intended to maintain one regulatable parameter at a specific level. The value of the level is known beforehand and it is set for a given system. All regulation takes place by the principle of deviation of the parameter being controlled from the set value. /229*

This approach can be considered to be true in the case, when all remaining systems of the organism function normally and only this system itself attempts to compensate for changes taking place in it. In the case of functioning of the entire complex of systems of the organism, change taking place in one of them simultaneously causes corresponding changes in the remaining ones. In this case, the entire complex comes to a state of equilibrium at other values of the parameters being regulated. The principle of rigid settings proves to be impracticable in this case. Thus, for example, regulation of arterial pressure in an organism is spoken of [4]. An attempt is made on this basis to create an artificial blood circulation apparatus, on the principle of holding arterial pressure constant. However, as experience shows, this

* Numbers in the margin indicate pagination in the foreign text.

apparatus frequently turns out to be unsuitable. On the other hand, some physiological data are evidence that there are cases, when pressure regulation in the organism is sacrificed in favor of supporting some other parameter. The case of increase in arterial pressure in hypertonic diseases is widely known, in which constriction of the vessels does not permit an adequate supply of blood to the organism, which leads to increasing the work of the heart and simultaneously causes an increase in pressure. The same thing takes place in hemorrhages. The pressure remains reduced for a long time, although the organism might sustain it at the normal level, by means of forced constriction of the vessels. An example also is known of complete rupture of the aorta, when the entire lower part of the organism was supplied by means of numerous connections in the blood circulation system, bypassing the aorta. The average arterial pressure of the patient was over 250 mm Hg and, nevertheless, the organism adapted to this pressure and functioned normally [5].

Thus, it is understandable from this example that any model of an isolated system describes its activity well in a quite limited range of change in the parameters. To extend the possibilities of use of models of physiological systems, a change has /230 to be made from modeling of isolated systems to models describing their combined functioning [6].

The discussion below is precisely about such a complex of physiological systems, associated with blood circulation [7]. The number of systems included in the complex is limited to five (these systems: lungs, internal and peripheral organs, centralization and redistribution of blood flow, heart). These five systems are sufficient for the complex to be closed. The entire operation of the complex is determined by one independent variable, namely, the degree of functional activity or, which is the same thing, the metabolism level, expressed by the amount of oxygen

consumed per unit time, in this case. There are two more independent variables in the complex, which characterize the external environment. These are the oxygen and carbon dioxide pressure in the air inhaled.

A model of the complex was assembled in an EMU-10 analog computer, and it includes 45 computing amplifiers, 12 multipliers and three nonlinearity blocks. A block diagram of the set is presented in Fig. 1.

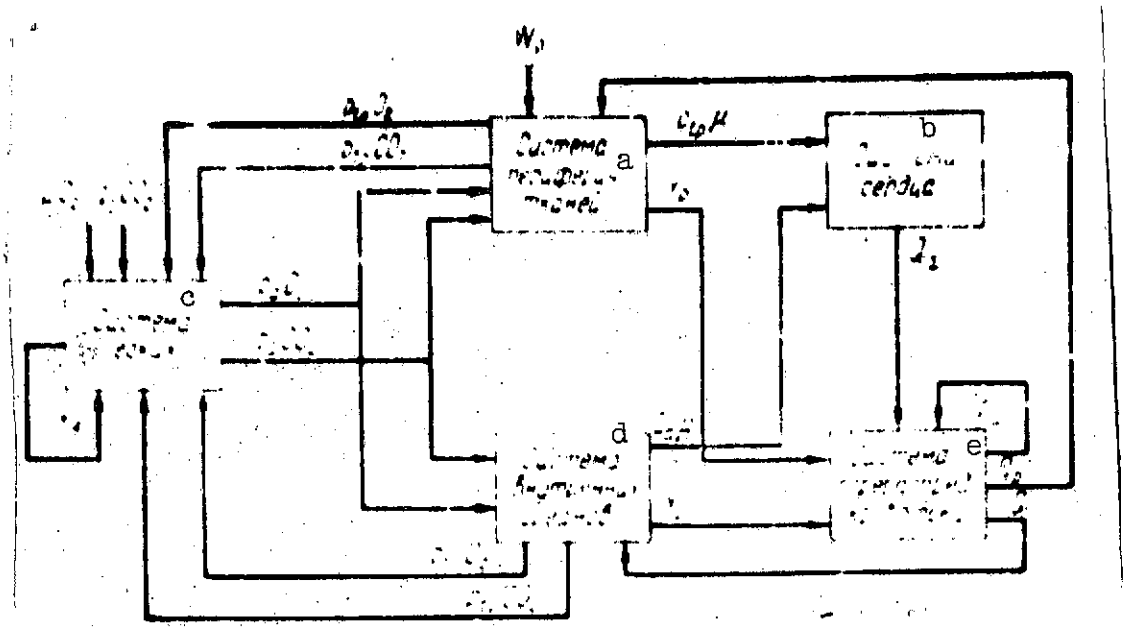

Fig. 1.

Key: a. Peripheral tissue system
b. Heart system
c. Lung system
d. Internal organ system
e. Blood redistribution system

The model is stable over the entire range of physiological activity, beginning with the state of rest and ending with conditions of intense stress on the organism. The static

characteristics of the model correspond well to known physiological data. Concerning the dynamics, the coincidence can be judged here, only on the basis of existing quite scanty data in the literature, such as, for example, the bioexponential nature of the blood flow recovery curve after severe physical stress [8].

Additional possibilities for improvement of the model and more exact definition of it dynamically; the properties are discovered by reproduction of several experiments, which are similar physiologically, using it. The conduct of such experiments also permits determination of the limits of adequacy of the model to the object. Those described below are among such experiments.

1. Forced Hypo- and Hyperventilation

For comparison of the results of modeling, the data of work [9] are used; they are presented in Table 1, together with data obtained with the model. The model experiment was set up in the following manner. The alveolar ventilation circuit V_A was interrupted, and the value of V_A was changed, without regard to the /231
source of stress. As is evident from the comparative table, the results of modeling coincide well with the results of a physiological experiment.

2. Test with Administration of Arfonad

Arfonad is a pharmacological agent, having a direct vasodilator effect [10]. A single intravenous injection of it, at a dose of 0.1-0.2 mg per kg of weight, causes rapid (in 1-2 min), brief reduction in arterial pressure (of 5-15 min) [11]. In this case, noticeable changes in the minute volume of the heart are not noted. Curves of change in diastolic and systolic pressure with administration of various doses of arfonad,

TABLE 1. GAS COMPOSITION OF ARTERIAL BLOOD AT VARIOUS LEVELS OF ALVEOLAR VENTILATION AND MODELING DATA

	V_A, ℓ/min	n	P_aO_2, mm Hg	P_aCO_2, mm Hg
Experiment [9]				
Normal ventilation	4.1	—	104	40
Alveolar hypoventilation	2.4		67	69
Alveolar hyperventilation	7.2		122	23
Modeling				
Normal ventilation	4.53	0.84	90	40
Alveolar hypoventilation	2.4	0.44	52	68
Alveolar hyperventilation	7.2	1.34	112	27

illustrating the Little test [12], are represented in Fig. 2a. A curve of the average arterial pressure can be plotted from the results of this test, by the well-known formula [13]

$$\overline{P}_A = P_d + 0.43(P_s - P_d).$$

A test in the model, illustrating arfonad administration, is conducted in the following manner. A voltage from an independent power supply source, the value of which corresponds to a certain concentration of arfonad, is supplied to the input of the peripheral conductivity block Y_p. In this case, the pressure decreases. On the basis of the scales adopted in the modeling system and the data of Fig. 2a, the voltage at the independent power source output is calibrated, corresponding to a certain amount of arfonad administered; in this case, the scale is 20 V/ /1 mg.

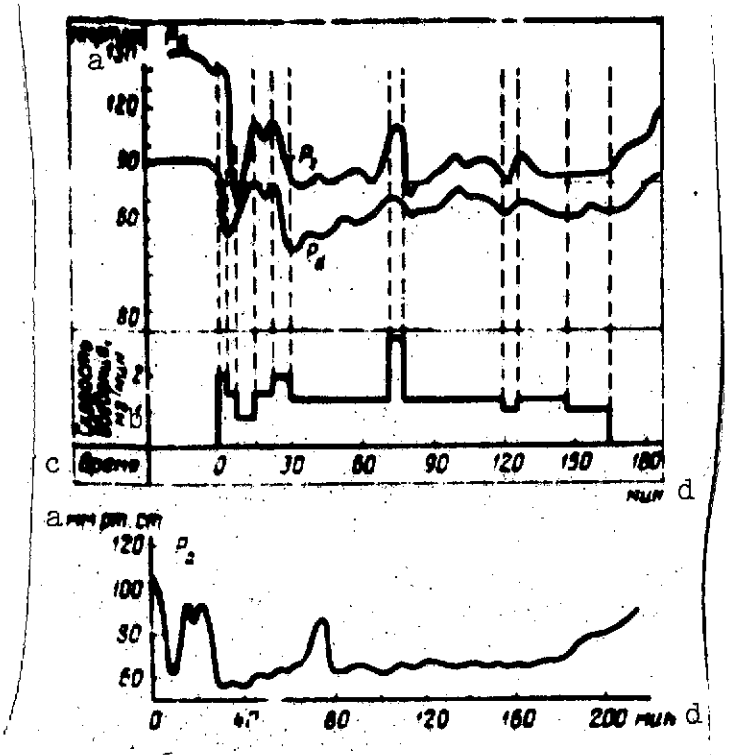

Fig. 2a. Change in arterial pressure upon administration of arfonad.

Key: a. mm Hg; b. Oxygen flow rate, mg/min; c. Time; d. Min

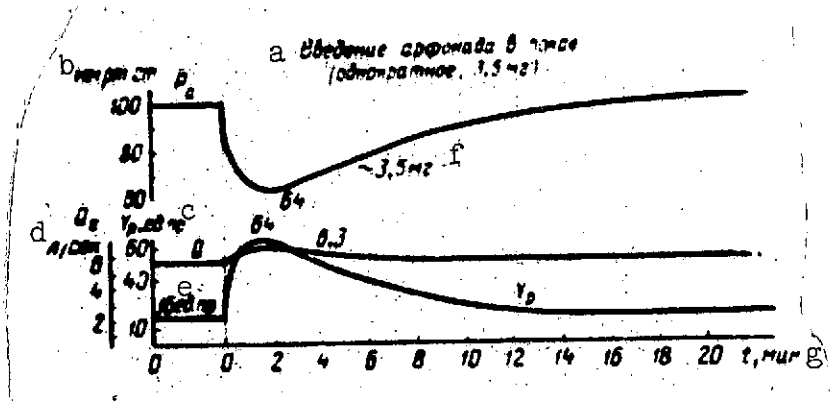

Fig. 2b. Administration of arfonad at rest (once, 3.5 mg).

Key: a. Arfonad administration at rest (single, 3.5 mg); b. mm Hg; c. Y_p, conductivity units; d. $\overline{Q}_\Sigma$, ℓ/sec; e. 16 conductivity units; f. ~3.5 mg; g. t, min

Curves of pressure $\overline{P}_A$, peripheral resistance Y_p and blood flow volume $\overline{Q}_\Sigma$, illustrating one-time administration of arfonad under rest conditions are presented in Fig. 2b (the value of Y_i is practically unchanged in this case).

The conductivity of peripheral tissues Y_p changes by four times in this case and the pressure drops by 36%. The blood flow changes negligibly (from 5.4 to 6.3 ℓ/min), i.e. by 16.7%. /233 Fig. 2c corresponds to the same test under conditions of intense work (equal to 50% of the maximum possible). The concentration of arfonad there causes an increase in Y_p of 55% overall and a 19% drop in average pressure. The minute volume is practically unchanged (3% of the minute volume under stress conditions). Fig. 2d illustrates the change in pressure with a

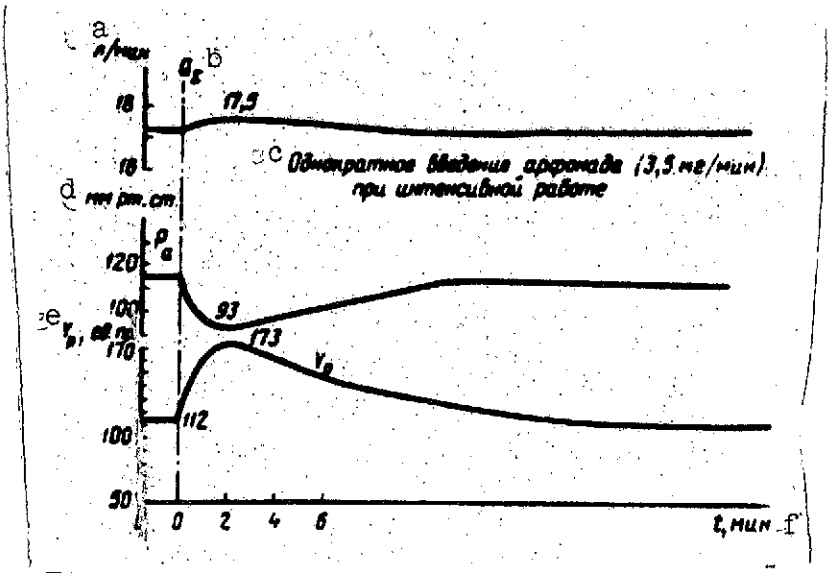

Fig. 2c. Single administration of arfonad (3.5 mg/min) during intense work.

Key: a. /min; b. $\bar{Q}$; c. Single administration of arfonad (3.5 mg/min) during intensive work; d. mm Hg; e. Y_p, conductivity units; f. t, min

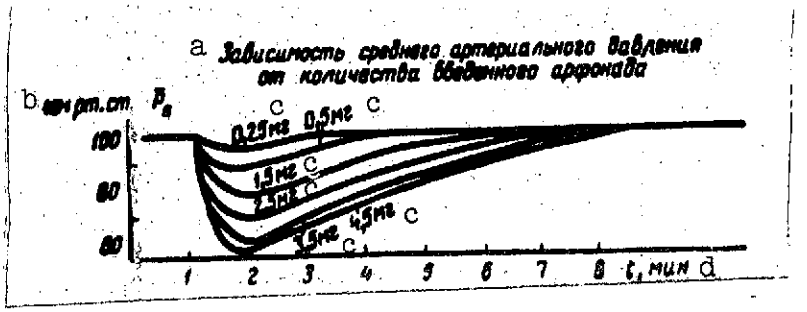

Fig. 2d. Average arterial pressure vs. amount of arfonad administered.

Key: a. Average arterial pressure vs. amount of arfonad administered; b. mm Hg; c. [illegible] mg; d. t, min

single administration of various doses of arfonad. The nonlinear dependence of pressure on arfonad concentration is seen well in this figure; with increase in arfonad dose to a value of 4-5 mg, saturation takes place, so that further increase in concentration in the blood does not lead to a corresponding reduction in pressure.

3. Modeling Test of Isolated Perfusion of Carotid Sinus

The carotid sinus is the name of a complex nerve formation, located in the area of branching of the common carotid artery into the outer and inner ones, and it is intended for reflex regulation of blood circulation. Normally, when the carotid sinus is included in the blood circulation, the pressure in it is approximately 100-120 mm Hg. If the region of the carotid sinus is isolated from the common vascular circulatory system and it is perfused separately, preserving the normal nerve connections in

this case, the effect of these connections on the organism can be traced. When the pressure in the region perfused is maintained at a level of 100-120 mm Hg, the carotid sinus has no effect. With an increase in pressure in the carotid sinus region, the pressure in the common circulatory system decreases and, with a decrease, increases [14], having a characteristic bend, which, in our opinion, is determined by the limited capacity of the heart to perform increased work under conditions of severe hypertonia.

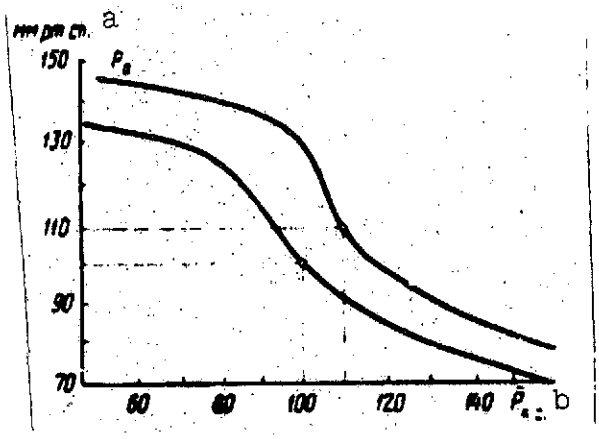

Fig. 3.
Key: a. mm Hg; b. $\bar{P}_{cs}$

This experiment was performed in the model in the following manner. The pressure in the region of perfusion of the carotid sinus was supplied from an independent voltage source, the output of which was connected, with appropriate coefficients, to the inputs of the amplifiers simulating Q_i and Y_Σ. The value of Q_i and Q_p are determined directly in this case by Y_i, Y_p and P_A in the organism (the subscripts i and p refer to the internal organs and peripheral tissues, respectively).

The results of the model and physiological curves are represented in Fig. 3. It must be noted here that such an experiment is considerably more complicated in practice, since, besides the carotid sinus reflex, there are several other mechanisms affecting the trend of the pressure curve, and there also is another series of baroreceptor areas. In our case, all baroreceptor areas were combined into one, as it were, and possible other mechanisms were not taken into account. As a result,

a static dependence is obtained, which does not change in the model, however long the experiment.

4. Effect of Different Methods of Regulation of an Artificial Heart

A natural heart in an intact organism reacts finely to all changes associated with the constantly changing metabolic requirements of the organism. An algorithm of this control still has not been completely elucidated [15]. It is only known that both /234 neural and hormonal mechanisms participate in regulation of cardiac activity. In the model being considered, the nerve connections are simulated by the combined baroreceptor block and the chemoreceptor block in the tissues, and the hormonal ones, by the arterial concentration of incompletely oxidized products block.

In modeling the working of an artificial heart, duplicating of the natural working mechanisms of the biological heart is not possible. Therefore, other methods are sought for control of the artificial heart [16]. Such methods can be tested, by including an artificial heart in the model. The simplest control algorithm, of the type $Q = \alpha_t z_1 \cdot \beta_t$, was chosen in this experiment. The following parameters were selected as the controlling signals: arterial concentration of incompletely oxidized products of metabolism, tissue concentration of these same products, alveolar ventilation and average arterial pressure. The values of coefficients α_t and β_t are presented in Table 2.

Algorithms 1-3 are stable over the entire range of functional activity of the organism. Algorithm 4 proved to be stable only in a limited range (blood flow 4.5-8 ℓ/min).

Algorithms 1 and 2 provided the closest to the initial flow of processes in the complex; however, direct use of concentration

TABLE 2

No.	Control algorithm	x	β
1	$Q_\Sigma = x_t C_t \mu + \beta_t$	$x_t = 0.157$ ℓ/min mg%	$\beta_t = -0.183$ ℓ/min
2	$Q_\Sigma = x_a C_a \mu + \beta_a$	$x_a = 0.183$ ℓ/min mg%	$\beta_a = 2.67$ ℓ/min
3	$Q_\Sigma = x_V V_A + \beta_V$	$x_V = 0.163$	$\beta_V = 2.37$ ℓ/min
4	$Q_\Sigma = x_P P_a + \beta_P$	$x_P = 0.050$ ℓ/min mm Hg	$\beta_P = 0$

of incompletely oxidized products of metabolism in both the tissue and in the blood meets with procedural difficulties. Therefore, it is advisable to attempt to discover some parameters, indirectly connected with change in these products and accessible for measurement.

Algorithm 3 also provides adequacy of blood circulation in all steady-state modes. However, in this case, the rate of establishment of the blood flow will be determined by the time constant of establishment of respiration, which is 3-4 times greater than in the blood circulation system. Moreover, fluctuating pressures are observed in the system during the transition process. It is interesting to note that this algorithm corresponds to that proposed in work [16], to some extent.

Conclusions

The results of the first tests on a model complex of interconnected physiological systems are reported in the paper. The purpose of reproducing similar experiments in the model is

determination of the limits of its usability and adequacy, as well as more precise definition of those of its parameters, which cannot be determined without these experiments. In part, such experiments can already find practical use. This concerns, in particular, modeling of algorithms of artificial heart control, the simplest of which were discussed in this work.

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